<795>: Adding Flavor to Conventionally Manufactured Nonsterile Products

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Disclaimer: This document is intended to be a resource regarding adding flavor to conventionally manufactured nonsterile products. This informational document is intended to supplement *USP* General Chapter <795> *Pharmaceutical Compounding – Nonsterile Preparations*. This supplemental document is not part of the chapter, is not a comprehensive overview of the chapter, and is not intended to be used in place of the chapter. This document is not official *United States Pharmacopeia – National Formulary* (*USP–NF*) text and is not intended to be enforceable by regulatory authorities. Users must refer to the *USP–NF* for official text.

Questions may be sent to CompoundingSL@USP.org.

Background and Introduction

USP General Chapter <795> *Pharmaceutical Compounding — Nonsterile Preparations* provides official standards for compounding quality nonsterile preparations. Nonsterile compounding is defined as combining, admixing, diluting, pooling, reconstituting other than as provided in the manufacturer's labeling, or otherwise altering a drug product or bulk drug substance to create a nonsterile preparation.

Adding components (such as flavors) not stipulated in the labeling to conventionally manufactured products is compounding and has been within the scope of <795> since the chapter was first published in 2004. Flavors are organic chemicals with reactive functional groups including acids, alcohols, aldehydes, amides, amines, esters, ketones, and lactams. The effect of adding these substances, even in very small quantities or concentrations, to conventionally manufactured products is unpredictable due to the potential for a variety of chemical reactions.

Assigning Beyond-Use Dates (BUDs)

BUD limits in <795> are based on the ability of a preparation to maintain chemical and physical stability and to suppress microbial growth. In the absence of stability data, BUDs must not exceed any of the following: manufacturers' recommendations, expiration date(s) of component(s), and BUD limits in <795>. In addition to stability data, aqueous preparations require passing antimicrobial effectiveness testing (see *Antimicrobial Effectiveness* Testing <51>) to extend BUDs beyond <795> BUD limits.

Table 1. BUD Limit by Type of Preparation in the Absence of a *USP–NF* Compounded Preparation Monograph or CNSP-Specific Stability Information[a]

Type of Preparation	BUD (days)	Storage Temperature[b]
Aqueous Dosage Forms ($a_w \geq 0.60$)		
Nonpreserved aqueous dosage forms[c]	14	Refrigerator
Preserved aqueous dosage forms[c]	35	Controlled room temperature or refrigerator
Nonaqueous Dosage Forms ($a_w < 0.60$)		
Oral liquids (nonaqueous)[d]	90	Controlled room temperature or refrigerator
Other nonaqueous dosage forms[e]	180	Controlled room temperature or refrigerator

[a] A shorter BUD must be assigned when the physical and chemical stability of the CNSP is less than the BUD limit stated in the table (see *10.4 CNSPs Requiring Shorter BUDs*).
[b] See *Packaging and Storage Requirements* <659>.
[c] An aqueous preparation is one that has an $a_w \geq 0.6$ (e.g., emulsions, gels, creams, solutions, sprays, or suspensions).
[d] A nonaqueous oral liquid is one that has an $a_w < 0.6$.
[e] Other nonaqueous dosage forms that have an $a_w < 0.6$ (e.g., capsules, tablets, granules, powders, nonaqueous topicals, suppositories, and troches or lozenges).

Documentation Requirements

Documentation may be written or electronic and must include:

- **SOPs** on each aspect of the compounding operation, QA and QC programs, and identity of designated person(s)
- **Personnel Training and Competency Assessments** as applicable to assigned tasks
- **Master Formulation Record** for each unique formulation
- **Compounding Record** each time a preparation is compounded
- **Component** receipt
- **Temperature** monitoring of storage area(s)
- **Cleaning and Sanitizing** logs

Summary

The requirements in <795> must be followed, including when adding flavor to conventionally manufactured nonsterile products, to minimize harm, including death, to human and animal patients that could result from 1) excessive microbial contamination, 2) variability from the intended strength of correct ingredients (e.g., ±10% of the labeled strength), 3) physical and chemical incompatibilities, 4) chemical and physical contaminants, and/or 5) use of ingredients of inappropriate quality.

Please refer to <795> *Pharmaceutical Compounding — Nonsterile Preparations* for complete requirements. Questions may be sent to CompoundingSL@USP.org.